

· 论 著 ·

妊娠期糖尿病患者阴道微生态和糖脂代谢水平与妊娠结局的相关性

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摘要: **目的** 探讨妊娠期糖尿病(GDM)患者阴道微生态、糖脂代谢水平,及其与妊娠结局的相关性。**方法** 选取2019年1月至2022年10月在宁德市医院就诊的150例GDM患者为观察组,另选取70例同期体检健康的正常妊娠孕妇为对照组。检测所有孕妇的阴道微生态、糖脂代谢水平。Logistic回归分析GDM患者妊娠结局不良的影响因素。**结果** 观察组患者阴道微生态失衡率高于对照组[59.33%(89/150) vs 21.43%(15/70), $\chi^2 = 27.511, P < 0.01$]。观察组三酰甘油(TG)、总胆固醇(TC)、空腹血糖、低密度脂蛋白胆固醇(LDL-C)、胰岛素、糖化血红蛋白(HbA1c)、肿瘤坏死因子- α (TNF- α)、白细胞介素-6(IL-6)、C反应蛋白(CRP)水平高于对照组,白蛋白水平低于对照组($P < 0.05$);两组阴道pH值比较差异有统计学意义($P < 0.05$)。观察组不良妊娠结局总发生率高于对照组,差异有统计学意义(34.67% vs 7.14%, $\chi^2 = 18.835, P < 0.01$)。Logistic回归分析显示,阴道微生态失衡及高水平的TC、空腹血糖、胰岛素、HbA1c、IL-6为GDM患者妊娠结局不良的独立影响因素($P < 0.01$)。**结论** GDM可导致孕妇糖脂代谢水平异常、阴道微生态失衡,进而可能影响妊娠结局。

关键词: 妊娠期糖尿病; 阴道微生态; 糖脂代谢; 妊娠结局; 糖化血红蛋白; 白细胞介素

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Correlation between vaginal microecology, glycolipid metabolism levels and pregnancy outcome in patients with gestational diabetes mellitus

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Abstract: Objective To investigate vaginal microecology, glycolipid metabolism levels in patients with gestational diabetes mellitus (GDM), and their correlation with pregnancy outcome. **Methods** A total of 150 GDM patients who received treatment at Ningde Municipal Hospital from January 2019 to October 2022 were selected as observation group, and other 70 healthy women with normal pregnancy were selected as the control group. The levels of vaginal microecology, glycolipid metabolism were detected. Logistic regression was used to analyze the adverse factors affecting pregnancy outcomes in GDM patients. **Results** The imbalance rate of vaginal microbiota in the observation group was higher than that in the control group [59.33% (89/150) vs 21.43% (15/70), $\chi^2 = 27.51, P < 0.01$]. Compared with control group, observation group had higher levels of triglycerides (TG), total cholesterol (TC), fasting blood glucose, low-density lipoprotein cholesterol (LDL-C), insulin, glycosylated hemoglobin (HbA1c), tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6) and C-reactive protein (CRP), and had lower level of albumin ($P < 0.05$). There was a significant difference in vaginal pH between the two groups ($P < 0.05$). The total incidence of adverse pregnancy outcomes in the observation group was higher than that in the control group (34.67% vs 7.14%, $\chi^2 = 18.835, P < 0.01$). Logistic regression analysis showed that vaginal microbiota imbalance, as well as high level of TC, fasting blood glucose, insulin, HbA1c and IL-6 were the independent influencing factors for poor pregnancy outcomes in GDM patients. **Conclusion** GDM can lead to abnormal glycolipid metabolism levels in pregnant women, as well as imbalance in vaginal microbiota, which may affect

pregnancy outcomes.

Keywords: Gestational diabetes mellitus; Vaginal microecology; Glycolipid metabolism; Pregnancy outcome; Glycosylated hemoglobin; Interleukin

妊娠期糖尿病 (gestational diabetes mellitus, GDM) 是一种常见的妊娠期慢性疾病,可能是由胰腺 β 细胞功能失调或与葡萄糖稳态相关的妊娠激素和肽分泌改变引起,与妊娠并发症、早产、先天性畸形等不良妊娠结局有关^[1-2]。糖尿病患者会出现糖脂代谢紊乱现象,影响患者机体正常生理功能,还可能诱发多种疾病。而空腹血糖和脂质代谢对 GDM 的预测具有重要的临床价值,有利于早期识别该疾病,降低母婴并发症的发病率,可能改善妊娠结局^[3]。因此有效改善孕妇糖脂代谢对孕妇健康及妊娠结局具有重大意义。此外,育龄妇女的阴道菌群失衡,可能增加生殖器感染、盆腔炎和不良妊娠结局的风险^[4]。阴道微生态是由阴道内正常菌群、机体的内分泌调节和解剖结构共同构成,阴道微生态失衡会导致免疫系统受损,外来微生物入侵生殖道从而引发炎症,可能促进生殖道疾病的进展^[5]。有研究表明,阴道微生态正常女性临床妊娠率高于阴道微生态异常女性,阴道微生态学的评估对于预测不孕妇女的辅助生殖结局可能具有重要价值^[6]。阴道微生物群对生态失调、女性健康、健康怀孕及妊娠结局等起着至关重要的作用^[7]。但目前关于 GDM 患者阴道微生态、糖脂代谢水平变化影响妊娠结局的研究相对较少,因此本研究主要分析 GDM 患者阴道微生态、糖脂代谢水平与妊娠结局的相关性及临床意义。

1 资料与方法

1.1 研究资料 选取 2019 年 1 月至 2022 年 10 月在宁德师范学院附属宁德市医院就诊的 150 例 GDM 患者为观察组,年龄 (27.94 ± 6.12) 岁,孕前身体质量指数 (body mass index, BMI) (22.14 ± 3.26) kg/m^2 ,孕次 (2.08 ± 0.51) 次;另选取 70 例同期体检健康的正常妊娠孕妇为对照组,年龄 (27.86 ± 6.07) 岁,孕前 BMI (22.08 ± 3.35) kg/m^2 ,孕次 (2.10 ± 0.51) 次。两组一般资料比较差异无统计学意义 ($P > 0.05$)。纳入标准:观察组符合 GDM 相关诊断标准^[8];自然受孕,且为单胎妊娠;孕周 > 28 周;近期末使用激素、抗生素类药物或免疫抑制剂;临床资料完整,患者签署同意书;无其他妊娠期疾病。排除标准:重要脏器功能异常;免疫系统疾病;不适宜进行阴道分娩或阴道试产胎儿风险较大;既往糖尿病史;甲状腺功能异常;病毒性感染;前置胎盘等并发症。研究

通过本院的伦理委员会批准通过。

1.2 研究方法

1.2.1 菌群检测 采用无菌棉拭子在阴道后穹窿处采集阴道分泌物,进行 pH 值、过氧化氢、唾液酸苷酶、白细胞酯酶、脯氨酸氨基肽酶和乙酰氨基葡萄糖苷酶检查,任一指标检查结果异常即为阴道微生态失衡^[9]。根据检查结果可对滴虫性阴道炎 (trichomonal vaginitis, TV)、细菌性阴道病 (bacterial vaginosis, BV)、外阴阴道念珠菌病 (vulvovaginal candidiasis, VVC) 及其他类型阴道炎 (淋球菌、支原体或衣原体感染等) 进行诊断;诊断标准及方法参考周芳芳等研究^[10]。

1.2.2 糖脂代谢指标及炎症因子比较 全部孕妇在入院当日清晨采集空腹静脉血 5 mL, 3 000 r/min, 离心半径 13.5 cm, 离心 10 min, 后收集血清。检测三酰甘油 (triglyceride, TG)、总胆固醇 (total cholesterol, TC)、高密度脂蛋白胆固醇 (high-density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇 (low-density lipoprotein cholesterol, LDL-C)、空腹血糖、胰岛素、糖化血红蛋白 (glycosylated hemoglobin, HbA1c)、白蛋白及 C 反应蛋白 (C-reactive protein, CRP)、肿瘤坏死因子- α (tumour necrosis factor alpha, TNF- α)、白细胞介素 (interleukin, IL) 6 水平。

1.2.3 不良妊娠结局 观察两组孕妇妊娠结局。其中不良妊娠结局包括自然流产、早产、新生儿窒息、新生儿畸形、巨大儿、死胎等及一些病理妊娠和分娩并发症^[11]。

1.3 统计学方法 采用 SPSS 25.0 软件处理数据。计数资料以例 (%) 表示,采用 χ^2 检验;呈正态分布的计量资料以 $\bar{x} \pm s$ 表示,采用成组 t 检验;GDM 患者妊娠结局不良影响因素采用多因素 logistic 回归分析。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组孕妇临床资料比较 两组年龄、孕周、产次、孕前 BMI、孕次比较差异无统计学意义 ($P > 0.05$), 阴道 pH 值比较差异有统计学意义 ($P < 0.01$)。见表 1。

2.2 两组阴道微生态失衡情况比较 150 例观察组中有 89 例患者阴道微生态失衡,失衡率为 59.33%, 高于对照组的 21.43% ($P < 0.01$)。见表 2。

2.3 两组糖脂代谢水平及炎症因子比较 观察组

TG、TC、LDL-C、空腹血糖、胰岛素、HbA1c、IL-6、CRP、TNF-α水平高于对照组,白蛋白水平低于对照组($P < 0.05$)。两组孕妇 HDL-C 水平比较差异无统计学意义($P > 0.05$)。见表3。

2.4 两组孕妇不良妊娠结局比较 观察组不良妊娠结局总发生率显著高于对照组($P < 0.01$)。见表4。

2.5 GDM患者阴道微生态、糖脂代谢指标与妊娠结局的关系 150例GDM患者中,妊娠结局不良者52例,良好者98例。妊娠结局不良患者阴道pH值水平、阴道微生态失衡比例和TC、空腹血糖、胰岛素、HbA1c、IL-6水平均高于妊娠结局良好患者($P < 0.01$)。见表5。

2.6 Logistic回归分析GDM患者妊娠结局不良影响因素 以阴道pH值($>4.5 = 1, \leq 4.5 = 0$)、阴道微生态失衡(失衡=1,平衡=0)、TC(实测值)、空腹血糖(实测值)、胰岛素(实测值)、HbA1c(实测值)、IL-6(实测值)为自变量,以GDM患者妊娠结局(不良=1,良好=0)为因变量,进行logistic回归分析,结果显示,阴道微生态失衡和高水平的TC、空腹血糖、胰岛素、HbA1c、IL-6为GDM患者妊娠结局不良的影响因素($P < 0.01$)。见表6。

表1 两组临床资料比较 [例(%)]

Tab. 3 Comparison of clinical data between two groups [case(%)]

项目	观察组(n=150)	对照组(n=70)	χ^2 值	P 值
年龄(岁)			0.976	0.323
>29	75(50.00)	40(57.14)		
≤ 29	75(50.00)	30(42.86)		
孕周(周)			0.110	0.740
>32	85(56.67)	38(54.29)		
≤ 32	65(43.33)	32(45.71)		
产次(次)			2.333	0.127
≥ 2	70(46.67)	25(35.71)		
<2	80(53.33)	45(64.29)		
孕前BMI(kg/m ²)			0.732	0.392
≥ 24	80(53.33)	33(47.14)		
<24	70(46.67)	37(52.86)		
阴道pH值			15.100	<0.001
>4.5	85(56.67)	20(33.41)		
≤ 4.5	65(43.33)	50(71.43)		
孕次(次)			0.335	0.563
≥ 2	77(51.33)	33(47.14)		
<2	73(48.67)	37(52.86)		

表2 两组阴道微生态失衡情况比较 (例)

Tab. 1 Comparison of vaginal microecology imbalance between two groups (case)

组别	例数	TV	BV	VVC	TV+BV	BV+VVC	其他	合计 [例(%)]
观察组	150	15	18	8	5	7	36	89(59.33)
对照组	70	2	2	1	1	2	7	15(21.43)
χ^2 值								27.511
P 值								<0.001

表3 两组糖脂代谢水平及炎症因子比较 ($\bar{x} \pm s$)

Tab. 3 Comparison of glycolipid metabolism and inflammatory factors between two groups ($\bar{x} \pm s$)

项目	观察组(n=150)	对照组(n=70)	t 值	P 值
TG(mmol/L)	6.19±0.96	5.81±0.93	2.762	0.006
TC(mmol/L)	4.38±1.05	2.76±0.91	11.105	<0.001
HDL-C(mmol/L)	1.82±0.32	1.90±0.35	1.676	0.095
LDL-C(mmol/L)	2.87±0.78	2.61±0.74	2.340	0.020
空腹血糖(mmol/L)	5.62±0.58	4.35±0.49	15.863	<0.001
胰岛素(pmol/L)	147.85±28.24	89.43±21.62	15.331	<0.001
HbA1c(%)	6.28±1.13	4.95±1.01	8.403	<0.001
白蛋白(g/L)	28.37±4.82	30.02±4.97	2.342	0.020
IL-6(ng/L)	514.23±40.56	316.24±40.15	33.831	<0.001
CRP(mg/L)	2.26±0.79	1.98±0.72	2.517	0.013
TNF-α(ng/L)	10.74±1.57	10.23±1.58	2.240	0.026

表4 两组不良妊娠结局比较 (例)

Tab. 4 Comparison of adverse pregnancy outcomes between two groups (case)

组别	例数	产后出血	早产	胎盘早剥	胎儿窘迫	巨大儿	低出生体重儿	新生儿畸形	病理性黄疸	合计 [例(%)]
观察组	150	4	6	5	13	8	3	8	5	52(34.67)
对照组	70	1	1	1	1	0	0	0	1	5(7.14)
χ^2 值										18.835
P 值										<0.001

表5 GDM患者阴道微生态、糖脂代谢指标与妊娠结局的关系 [例(%)]

Tab. 5 Relationship between vaginal microecology, glycolipid metabolism and pregnancy outcome in GDM patients [case(%)]

项目	妊娠结局不良 (n=52)	妊娠结局良好 (n=98)	χ^2/t 值	P 值
阴道pH值 ^a				
>4.5	36(69.23)	49(50.00)	5.117	0.024
≤ 4.5	16(30.77)	49(50.00)		
阴道微生态失衡 ^a	42(80.77)	47(47.96)	15.157	<0.001
TC(mmol/L) ^b	4.92±1.06	4.10±1.05	4.537	<0.001
空腹血糖(mmol/L) ^b	6.31±0.58	5.26±0.58	10.552	<0.001
胰岛素(pmol/L) ^b	185.72±28.26	127.76±28.23	11.963	<0.001
HbA1c(%) ^b	6.97±1.13	5.92±1.13	5.416	<0.001
IL-6(ng/L) ^b	576.33±40.58	481.28±40.55	13.659	<0.001

注:^a为用例(%)表示;^b为用 $\bar{x} \pm s$ 表示。

表6 GDM患者妊娠结局不良影响因素的多因素分析

Tab. 6 Multivariate analysis of adverse factors of pregnancy outcomes in GDM patients

影响因素	β	SE	Wald	P 值	OR 值	95%CI
阴道微生态失衡	0.243	0.064	14.410	<0.001	1.275	1.125~1.445
TC	0.194	0.051	14.458	<0.001	1.214	1.099~1.342
空腹血糖	0.128	0.023	31.162	<0.001	1.137	1.087~1.189
胰岛素	0.118	0.030	15.414	<0.001	1.125	1.061~1.193
HbA1c	0.162	0.042	14.899	<0.001	1.176	1.083~1.277
IL-6	0.048	0.011	18.912	<0.001	1.049	1.027~1.072

3 讨论

3.1 相关指标水平和妊娠结局的关系 GDM传统上

是指在怀孕期间发病或首次识别的葡萄糖耐量异常,是妊娠常见的并发症之一,长期以来一直与产妇和新生儿并发症有关,被认为是未来母体及其后代的代谢性疾病和不良妊娠结局的危险因素;其患病率在国际上持续上升^[12]。GDM 涉及各种紊乱的代谢途径,包括氨基酸、碳水化合物、脂质和嘌呤^[13-14]。曾有研究表明,单胎和双胎妊娠并发 GDM 患者的脂质代谢特征不同,双胎妊娠并发 GDM 患者胰岛素抵抗加重,妊娠并发症较多,妊娠结局较差^[15]。史俊霞等^[16]研究表明,GDM 患者空腹血糖、TG、TC、LDL-C 水平较高,其不良妊娠结局发生率显著高于正常妊娠孕妇。GDM 患者 TNF- α 、IL-6、CRP 水平较高^[17]。在本研究中,观察组 TG、TC、空腹血糖、胰岛素、HbA1c、TNF- α 、LDL-C、IL-6、CRP 水平高于对照组,白蛋白水平低于对照组;妊娠结局不良患者 TC、空腹血糖、胰岛素、HbA1c、IL-6 水平高于妊娠结局良好患者。提示空腹血糖、TG、TC、LDL-C、TNF- α 、IL-6、CRP 等指标可能参与了 GDM 的病理生理过程,可能与其妊娠结局密切相关。

3.2 GDM 患者妊娠结局不良的影响因素 阴道微生物生态状况是女性生殖健康的重要指标。阴道和子宫微生物群变化可能会导致微生态失调,出现菌群失衡、炎症反应和免疫反应异常等,都与女性健康状况不佳和不良妊娠及新生儿结局的风险增加有关^[18-19]。Witkin 等^[20]研究证明了女性生殖道微生物群在预测和预防早产中具有重要作用。裘萧灵等^[21]研究表明,GDM 患者微生态失调率较高,阴道微生态失调的 GDM 患者不良妊娠结局发生率高于微生态正常者。郭珍等^[22]研究表明,GDM 组阴道微生态异常发生率高于对照组,两组孕妇不良妊娠结局发生率比较差异有统计学意义。在本研究中,150 例观察组中阴道微生态失衡率为 59.33%,高于对照组的 21.43%,两组孕妇阴道 pH 值比较差异有统计学意义;观察组不良妊娠结局总发生率高于对照组;Logistic 回归分析显示,阴道微生态失衡及高水平的 TC、空腹血糖、胰岛素、HbA1c、IL-6 为 GDM 患者妊娠结局不良的独立影响因素。

综上所述,GDM 患者糖脂代谢水平异常、阴道微生态失衡,可能增加不良妊娠结局发生风险;控制阴道微生态及糖脂代谢指标可能对降低不良妊娠结局发生率具有一定作用。但本研究样本量较少,且阴道微生态及糖脂代谢指标影响 GDM 具体作用机制尚不明确,未来需纳入更多样本量进一步分析。

利益冲突 无

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